Acute Pancreatitis Complicated with Transient Portal Venous Thrombosis in One Patient with Hepatocellular Carcinoma and Cirrhosis

Hugo You-Hsien Lin,[1] Zu-Yau Lin,[1,3] Paul Ming-Chen Shih,[2] and Wan-Long Chuang[1,3]
[1]Division of Hepatobiliary Medicine, Department of Internal Medicine, and [2]Department of Radiology, Kaohsiung Medical University Hospital, and [3]Department of Internal Medicine, Faculty of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan.

Portal venous thrombosis (PVT) is a condition associated with high morbidity. The etiologies of PVT include intra-abdominal inflammation or infection, surgical intervention, abdominal malignancies such as hepatocellular carcinoma (HCC) and pancreatic carcinoma, or abnormality in coagulation caused by various reasons such as liver cirrhosis. Management of PVT should be based on its etiology and the condition of the patient. We describe a cirrhotic patient with HCC who suffered from acute pancreatitis. PVT in the main trunk was detected at admission due to the episode of acute pancreatitis. The etiology of thrombosis was considered to be inflammation around the main portal trunk caused by pancreatitis rather than cirrhosis or HCC. We did not instigate any management for the thrombosis. Acute pancreatitis was relieved after conservative treatment. Follow-up imaging study performed 46 days after detection of thrombosis showed spontaneous complete resolution of the thrombus. Our experience may provide useful information for the management of such patients.

Key Words: hepatocellular carcinoma, liver cirrhosis, pancreatitis, portal venous thrombosis
(*Kaohsiung J Med Sci* 2007;23:254–8)

Portal venous thrombosis (PVT) may be primary or secondary in origin [1–4]. Secondary PVT can be caused by various acquired disorders such as antithrombin III deficiency, sepsis, disseminated intravascular coagulation, intra-abdominal infectious or inflammatory conditions, liver cirrhosis, surgical intervention, or abdominal malignancies such as pancreatic or hepatocellular carcinoma (HCC). Symptom development in PVT is often insidious and related to the progression of portal hypertension which can lead to hemorrhage from esophageal or cardiac varices. Moreover, malignant PVT can cause wide dissemination of cancer cells. Management of PVT should be based on its etiology and the condition of the patient, e.g. anticoagulation therapy for benign PVT, and treatment of underlying cancer for malignant PVT. However, the side effects of treatment cannot be tolerated by some of these patients. In this case report, a cirrhotic patient with HCC suffered from acute pancreatitis complicated with transient PVT in the main trunk. Our experience may provide useful information for the management of such patients.

Received: October 23, 2006 Accepted: December 11, 2006
Address correspondence and reprint requests to: Dr Zu-Yau Lin, Division of Hepatobiliary Medicine, Department of Internal Medicine, Kaohsiung Medical University, 100 Tzyou 1st Road, Kaohsiung 807, Taiwan.
E-mail: linzuyau@yahoo.com.tw

Case Presentation

The patient was a 33-year-old man with HCC and liver cirrhosis caused by chronic hepatitis B virus infection. Multiple nodular type HCC was diagnosed based on high serum α-fetoprotein (AFP) level (3,296 ng/mL; normal < 20 ng/mL) [5] and imaging studies [6] in December 2004. He received three sessions of transcatheter arterial chemoembolization and one session of percutaneous pure ethanol injection for the management of HCC. The functional reserve of liver cirrhosis was maintained in Child–Pugh class A. Serum AFP level returned to within normal range after this treatment, but it rebounded to 165.9 ng/mL on March 22, 2006.

Serial imaging studies including whole body bone scan, chest X-ray, abdominal ultrasonography, magnetic resonance imaging and angiography were performed to detect the possibility of recurrent HCC. However, no definite viable HCC was found. The serum AFP level increased to 422 ng/mL on June 7, 2006. The condition of the patient was quite satisfactory until June 25, 2006 when he suffered severe abdominal pain and was sent to our emergency department. The characteristics of the pain were dull, radiating to the back, aggravated by food intake and relieved by bed rest. The location of the pain was around the epigastric area. Physical examination showed diffuse abdominal tenderness, diminished bowel sounds but no rebounding pain or fever. Laboratory data showed serum C-reactive protein 15.32 μg/mL (normal < 5 μg/mL), amylase 308 U/L (normal < 123 U/L), lipase 284 IU/L (normal < 58 IU/L), aspartate aminotransferase 51 U/L (normal < 35 U/L), alanine aminotransferase 66 U/L (normal < 92 U/L), total bilirubin 2.13 mg/dL (normal < 1.11 mg/dL), and conjugated bilirubin 1.17 mg/dL (normal < 0.4 mg/dL). The coagulation profile was: prothrombin time, 11.6 seconds/10.7 seconds (control); international normalized ratio, 1.05; partial prothrombin time, 33.4 seconds/30.1 seconds (control).

Under the impression of acute pancreatitis, contrast-enhanced computed tomography (CT) was performed. Peripancreatic fluid collection around the pancreatic head was found, which supported the diagnosis of pancreatitis. Moreover, CT also showed deposition of lipiodol caused by previous transcatheter arterial chemoembolization in segments 3 and 6 by Couinaud Segmental Classification [7], suspected dysplastic nodules in segments 5 and 6 [7], liver cirrhosis with splenomegaly, gallbladder stones, main portal trunk thrombosis, and ascites (Figure 1).

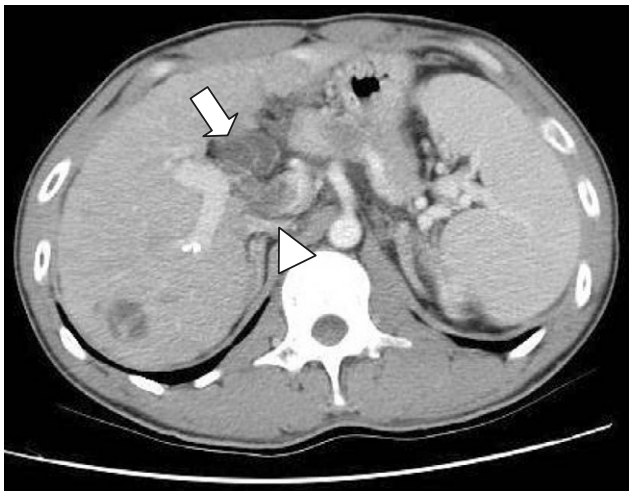

Figure 1. *Contrast-enhanced computed tomography in this slice showed peripancreatic fluid collection (arrow) around the pancreatic head and thrombosis of the main portal trunk (arrowhead) that was not detected by magnetic resonance imaging performed 1 month previously. This slice also showed deposition of lipiodol in segments 3 and 6, a suspected dysplastic nodule in segment 6, liver cirrhosis with splenomegaly and collateral circulation at the splenic hilum and perigastric region.*

He was admitted to our institution for the treatment of acute pancreatitis. The general condition of the patient improved rapidly after conservative management and he was discharged 9 days later. Reserve liver function did not deteriorate during admission. The main portal trunk thrombosis was not treated because thrombosis was considered to be caused by local inflammation during the episode of pancreatitis and observation was advised.

Unfortunately, he suffered from another similar episode of severe abdominal pain on August 10, 2006. The characteristics of the pain were dull, radiating to the back, aggravated by food intake and relieved by bed rest. The location of the pain was around the epigastric area. Physical examination showed diffuse abdominal tenderness, decreased bowel sounds but no rebounding pain or fever. Laboratory data showed an elevated serum lipase level (215 IU/L). Under the impression of acute pancreatitis, contrast-enhanced CT was again performed. Compared to the previous study, the amount of ascites had slightly increased. The sizes of the hepatic nodules remained unchanged and the main portal trunk was free of thrombosis

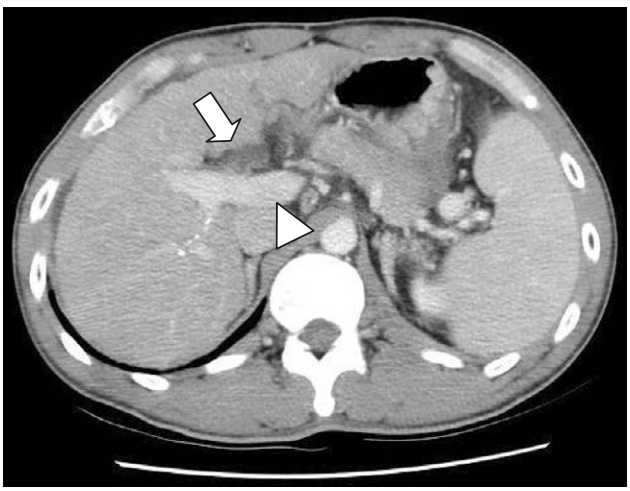

Figure 2. *Compared to the previous contrast-enhanced computed tomography, the amount of peripancreatic fluid collection (arrow) around the pancreatic head had decreased, but ascites had slightly increased. The main portal trunk was free of thrombosis (arrowhead).*

(Figure 2). He was admitted to our institution for conservative treatment of acute pancreatitis and discharged 7 days later.

Discussion

Liver cirrhosis plays an important role in adult patients with PVT. Splenomegaly, wide main portal trunk, high portal venous pressure and the terminal stage of liver function are reported to be risk factors for the development of PVT in patients with cirrhosis [8,9]. However, the actual mechanism for the development of PVT in patients with cirrhosis still needs to be clarified [10]. It has been reported that a decrease in portal blood flow and the presence of peripheral lymphangitis and fibrosis may be associated with the development of PVT [11]. Reduced liver synthetic activity made the coagulation and anticoagulation factors abnormal in patients with liver cirrhosis [12]. Abnormality in coagulation can be a precipitating factor for the development of PVT.

Neoplasm is another important cause of the development of PVT. Among malignancies causing PVT, HCC and pancreatic carcinoma are the two most frequent causes [13]. The mechanisms for the development of PVT in malignancy can be due to the invasion of cancer cells to the portal lumen, compression of the portal vein by tumor burden, or by neoplasm-related prothrombotic changes [14].

Management of PVT should be based on its etiology and the condition of the patient. Spontaneous resolution of PVT caused by benign etiology is possible but uncommon [13]. Anticoagulation therapy is recommended for the treatment of acute benign PVT as complete or partial resolution can be achieved in up to 80% of patients [15]. Heparin and tissue-type plasminogen activator (t-PA) are used in most studies [15–17]. Anticoagulation may not increase the risk of bleeding but reduces that of mesenteric infarction, which is possibly life-threatening. However, systemic anticoagulation therapy may be unsuitable for cirrhotic patients with severe abnormality in coagulation. Thrombolysis through a transhepatic route is another choice for the treatment of acute benign PVT to avoid the adverse effects of systemic anticoagulant therapy [17–19]. This is an invasive management and carries the risk of intra-abdominal hemorrhage or hemobilia. The management of PVT caused by malignancy is quite different from that used for the management of benign PVT. The resolution of malignant PVT can be achieved only when the involved cancer cells can be well treated. Systemic chemotherapy, local irradiation therapy, or transcatheter arterial chemoembolization are choices for the management of malignant PVT. However, each of the above carries its own side effects and cannot be applied to all patients with malignant PVT.

The case presented above had HCC and cirrhosis, both of which could possibly develop to PVT. Progressive increase in serum AFP levels during the follow-up period strongly suggested recurrence of HCC. Therefore, new-onset PVT detected by CT was reasonably considered to be malignant in origin. However, the location of PVT was in the main trunk. There was no detectable hepatofugal portal flow in imaging studies and the other parts of the portal system were completely free of thrombosis. The locations of all treated HCC nodules and the suspected dysplastic nodules were far away from the main trunk thrombus. There was also no detectable tumor burden around the main portal trunk. PVT in this case was not considered to be caused by HCC. On the other hand, the possibility of PVT caused by cirrhosis could not be completely excluded. However, this case did not have past history of abnormality in coagulation. Sudden onset of thrombosis located only in part of the main trunk was not easily explained by the reason of abnormality in coagulation. Pancreatitis is a possible etiology of PVT. The mechanism is suggested to be either portal venous

compression caused by pseudocyst or abscess, or an imbalance between blood coagulation and fibrinolysis [19]. Portal phlebitis caused by leakage of pancreatic juice around the portal vein may also be a factor in the development of PVT in pancreatitis. The location of thrombus in this case was surrounded by the fluid induced by the episode of pancreatitis. Formation of thrombus caused by local phlebitis was the most reasonable explanation in this case. PVT can elevate the portal pressure which had the potential to cause rupture of esophageal or cardiac varices. In this case, we did not examine the change in portal pressure or varices during admission, because there was no evidence of gastrointestinal hemorrhage to support the necessity of performing further examination. We did not treat the PVT and chose close observation instead. Disappearance of thrombus soon after recovery from acute pancreatitis confirmed that PVT was caused by the inflammatory process. The second episode of acute pancreatitis did not show evidence of PVT. This could be explained by fluid collection around the main trunk in the second episode being much less than that in the first episode. Two episodes of acute pancreatitis could be successfully treated by a conservative approach. No obvious cause of pancreatitis could be identified by imaging studies, patient drug abuse history, or laboratory data. Although the imaging studies did not show any evidence of biliary stones, according to the clinical course of this patient, pancreatitis caused by passage of common bile stones combined with or without cholangitis was the most likely etiology.

In conclusion, PVT can be caused by pancreatitis. Control of the underlying disease may be the first choice for treatment of this kind of PVT. Development of PVT in a patient with HCC and cirrhosis necessarily originates from one of these two possible etiologies and the other possibilities should also be considered.

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合併肝癌肝硬化病人因急性胰臟炎產生暫時性門靜脈栓塞 — 個案報告

林祐賢[1] 林子堯[1,3] 石明誠[2] 莊萬龍[1,3]

高雄醫學大學附設醫院 [1]肝膽胰內科 [2]放射線科

[3]高雄醫學大學 醫學院醫學系 內科

門靜脈栓塞易導致高死亡率。造成門靜脈栓塞的原因包含了腹腔內發炎、感染、開刀、腹腔內惡性腫瘤 (如肝癌、胰臟癌)，與凝血機能障礙 (先天性疾病、肝硬化)，對治療門靜脈栓塞之方法並非一成不變且各有其可能出現之副作用，因此正確之治療須取決於其造成之原因與病人之情況。我們報告一位 33 歲男性併有肝癌、肝硬化因急性胰臟炎而產生暫時性門靜脈栓塞之個案。造成此門靜脈栓塞之原因推斷是因胰臟炎造成門靜脈血管發炎所致。對於門靜脈栓塞，我們採取密切追蹤之因應方式。在急性胰臟炎改善後，影像追蹤顯示門靜脈栓塞完全消失。我們的經驗可提供臨床醫師往後治療疑似此類病人之參考。

關鍵詞：肝癌，肝硬化，胰臟炎，門靜脈栓塞部

(高雄醫誌 2007;23:254－8)

收文日期：95 年 10 月 23 日

接受刊載：95 年 12 月 11 日

通訊作者：林子堯醫師

高雄醫學大學附設醫院肝膽胰內科

高雄市807三民區自由一路100號